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NOVAK DRUCE DELUCA & QUIGG, LLP			HIRIYANNA, KELAGINAMANE T	
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SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
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Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/549,684	WOHLRAB, DAVID	
	Examiner Kelaginamane T. Hiriyanna	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 19 September 2005.
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-14 and 16-21 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 1-14 and 16-21 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date <u>09/19/05</u> .	5) <input type="checkbox"/> Notice of Informal Patent Application
	6) <input type="checkbox"/> Other: _____

DETAILED ACTION

Claims 1-14 and 16-21 are pending and presently under examination.

Specification

Priority date for elected invention is applied under 35 USC§119(a-d) for the provisional Application No. GERMANY 10311889.6 filed on 03/18/2003.

Claim Objections

Claims 2-14 are objected to because of the following formalities: While claiming dependence on the subject of previous claim referring to "The" subject of previous claim is proper format. Accordingly, "Cell preperation" in claims 2-14 should read "The cell prperation". Appropriate correction is required.

Claims 20-21 are objected to because of the following formalities: While claiming dependence on the subject of previous claim referring to "The" subject of previous claim is proper format. Accordingly, "Method according to" in claims 20 & 21 should read "The method to". Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-14 are rejected under 35 U.S.C. 101 because claim is drawn to non-statutory subject matter as follows:

Claims 1-14 claims are drawn to 'Cell'. When read broadly this encompasses cells of intact live animals and humans. The insertion of a phrase such as "an isolated cell preparation", or "cultured mammalian cell preparation" would overcome this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 and all its dependent claims are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. The claims are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors.

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recitation "...the substance...is at least a local anaesthetic..." makes the claim vague and indefinite. It is unclear what is 'metes and bounds' of the claim in this context.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

"The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention."

Claims 1-15 and 16-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The scope of invention as claimed encompasses therapeutic and/or cosmetic compositions of any cell preparations comprising human or any animal cells which were cultivated using a generic substance or a mixture of any and/or all substances that activate the expression of CD44 in these cells. Instant claims further encompass compositions of said cells and said substances that are undefined with respect to amounts or proportions of the components and therapeutic compatibilities, and all

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derivatives and mixtures of a local anesthetic that activate CD44 expression, cell that are autologous, allogenic or xenogenic origin and cells originated from other cell systems by differentiation process.

The specification at best teaches compositions and use of compositions of chondrocyte cells isolated from human cartilage and expanded in vitro cultures in the presence of lidocaine (example 1). Applicant further broadly discloses the use of hyaluronic acid and a local anesthetic (lidocaine) in activating the expression of CD44 in cells. Given the state of the art, such broad guidance does not constitute the specific direction and guidance the artisan would require to reasonably predict that any cells can be used, that any substance can be used in inducing CD44 expression in cells.

The application does not disclose any other compositions of cells other than the mentioned above, does not describe any other substances or anesthetic substances or their derivatives other than lidocaine that can induces CD44 expression cells. Thus the number of examples or species does not commensurate with the scope and breadth of the instant claims.

Applicant is referred to the guidelines for *Written Description Requirement* published January 5, 2001 in the Federal Register, Vol.66, No.4, pp.1099-1110 (see <http://www.uspto.gov>). The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (See *In re Shokal* 113USPQ283(CCPA1957); *Purdue Pharma L. P. vs Faulding Inc.* 56 USPQ2nd 1481 (CAFC 2000). In analyzing whether the written description requirement is met for the genus claim, it is first determined whether a representative number of species have been described by their complete structure. Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics.

Since the specification fails to disclose other claimed compositions that contained sufficient number of examples of cell types and sufficient number of substances that induce CD44 expression in cell composition, it is not possible to envision the broadly claimed compositions and substances would provide the same results as chondrocyte cells expressing CD44 in presence of lidocaine and hyaluronic acid. One cannot

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describe what one has not conceived. (See *Fiddes v. Baird*, 30 USP2d 1481 at 1483). Therefore, the lack of disclosure in the specification is not deemed sufficient to reasonably convey to one skilled in the art that the applicants were in possession of the huge genera recited in the claims at the time the application was filed. Furthermore the possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. See, e.g., *Pfaff v. Wells Electronics, Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406; *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991). In the instant case the compositions as claimed has been defined only by a statement that broadly encompasses any cells and any substance that induces CD44 expression in said cells which conveyed no distinguishing information about the identity of the broadly claimed species of cells and/or substances. Accordingly one of skill in the art would conclude that applicant was not in possession of the claimed genus because a description of a single member of this genus would not be representative of claimed genus of substances and cell types and is insufficient to support the claim in its present scope. At the best the specification provides the enabled description of a composition and a method of use of compositions of compositions of chondrocyte cells isolated from human cartilage and expanded in vitro cultures in the presence of lidocaine.

Claims 1-14 and 16-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition of cell comprising isolated chondrocyte cells, lidocaine and hyaluronic acid and a method of producing and cultivation said cell prperation, does not enable a any other pharmaceutical compositions, does not enable any method of treating of any claimed disease or defects or disorder in human or other animals. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

At issue, under the enablement requirement of 35 U.S.C. 112, first paragraph is whether, given the Wands-factors, the experimentation was undue or unreasonable under the circumstances. "Experimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art." See *Fields v. Conover*, 443 F.2d 1386, 170 USPQ 276 (CCPA 1970). These factors include, but are not limited to: (1) The breadth of the claims; (2) The nature of the invention; (3) The state of the prior art; (4) The level of one of ordinary skill; (5) The level of predictability in the art; (6) The amount of direction provided by the inventor; (7) The existence of working examples; and (8) The quantity of experimentation needed to make or use the invention based of the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). All of the wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below as to show that one of the ordinary skill in the art have to go through "undue experimentation" in order to practice the invention.

Nature of the invention: The invention relates to methods of use of isolated cell compositions comprising cells and substances that induce CD44 expression said cells in treating therapeutically, prophylactically and/or metaphylactically the defects or degenerative diseases especially in a cartilaginous tissue in humans or animals.

Breadth of the claims And Guidance Provided in the Specification: The scope of invention as claimed encompasses a method of treatment, prophylaxis or metaphylaxis of degenerative diseases, cartilage and cartilage bone defects in animal joints, defects in meniscus and intervertebral discs, defects in skin humans or animals using compositions of a cell preparation comprising isolated human or any animal cells cultivated using a substance or mixtures of any and/or all substances that activate the expression of CD44 and hyaluronic acid and its derivatives as bonding agents. Instant claims further encompass compositions of said cells and said substances that are undefined with respect to amounts or proportions of the components and therapeutic compatibilities, and all derivatives and mixtures of a local anesthetic that activate CD44 expression, cells that are allogenic or xenogenic in origin and cells originated from other cell systems by differentiation process etc.

The specification at best teaches compositions and use of compositions of chondrocyte cells isolated from human cartilage and expanded in vitro cultures in the presence of lidocaine (example 1). Applicant further broadly discloses the use of certain substances in activating the expression of CD44 in cells and use of these cell compositions further comprising hyaluronic acid in treating and cosmetic applications. Given the state of the art, such broad guidance does not constitute the specific direction and guidance the artisan would require to reasonably predict that any cells can be used, that any substance can be used in inducing CD44 expression in cells.

The application does not enable compositions of cells other than chondrocyte and lidocaine that can induce CD44 expression in cultivated cells. Further the application does not enable a method of treating any conditions in humans or animals with said compositions.

In the absence of representative number of enabled examples in the specification commensurate with the breadth of the claims one of ordinary skill in the art would conclude that the invention is unpredictable and would require undue experimentation to practice the invention in its full scope. Applicants' attention is drawn to *In re Shokal*, 242 F.2d 771, 113 USPQ 283 (CCPA 1957). The test is whether the number of claimed genus/or species of cell types, CD44 inducing substances, derivatives of local anesthetic and etc., as instantly claimed and prior to the reference date or the date of the activity provided an adequate basis for inferring that the invention has generic applicability.

The level of one of ordinary skill in the Art at the Time of Invention: The level of one of ordinary skill in the art at the time of filing of the instant application is high requiring an advanced degree or training in the relevant field. The status of the art at the time of filing was such that said skilled in the art would not have been able to make or use the invention for its fully claimed scope without undue experimentation.

State of the Art, the Predictability of the Art: At about the effective filing date of the present application art is unpredictable with regard to use of any cells and use of allogeneic and xenogenic transplantations of any cell types. Given the unpredictability in the art, absent a strong showing by Applicant, in the way of specific guidance and

direction, and/or working examples demonstrating the same for sufficient number of claimed compounds and methods, such invention as claimed by Applicant is not enabled.

Amount of experimentation necessary: Because of the lack of working examples, insufficient guidance and direction provided by Applicant, the inherent unpredictability of the art, and the nature of the invention, one of skill in the art would be required to perform a large amount of experimentation to make and/or use the invention in its full scope as claimed by Applicant. Such experimentation would be required to identify the cell types that could be used for treating degenerative diseases, cartilage and cartilage bone defects in animal joints, defects in meniscus and intervertebral discs, defects in skin humans or any other animals. Further one of skill in the art to identify and characterize sufficient number of biocompatible substances that can induce CD44 expression in any cells. Further these claims are not enabled because one of skilled in the art, at the date of filing, would not be able to rely upon the state of the art in order to successfully predict a priori a substance that could induce CD44 expression cell when cultivated with it. Accordingly, in view of the lack of teachings in the art and lack of guidance provided by the specification with regard to an enabled therapeutic use of sufficient number of cell types and substance compositions that can induce CD44 expression in said cells in treating any degenerative cartilage or bone disease in humans and animals and as of around the filing date of instant application and for the specific reasons cited above, it would have required undue experimentation for one of skill in the art to make and use the full scope of the claimed invention. At the best the specification as filed is found only enabled for a composition of cell comprising isolated chondrocyte cells, local anesthetic lidocaine and hyaluronic acid.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application

filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-14 and 16-21 are rejected under 35 USC 102 (b) as being anticipated by Askhar et al., (WO 01/35968).

The above claims are directed to a making and using of compositions isolated cell preparation for therapeutic and cosmetic application in humans and animals containing a substance or mixtures of substances which activate CD44 expression to which cells hyaluronic acid or salts and fragments thereof are bonded.

Regarding claim 1; 3-5, 19 Askhar teaches cell preparation and a method which includes proliferating pluripotent mesenchymal cells and promoting expression of CD44 and chondrocytic differentiation in vitro cultures comprising chondrogenesis promoting agents (substances) and hyaluronic acid and more over the methods can be used to replace or augment cartilage tissue (see p.3, lines 12-31 bridging p.4, lines 1-17, p.24). Regarding claim 2 Askhar teaches using Hyaluronic acid at concentrations ranging from 10 ug/ml to 100 mg/ml (which is about 0.01%-10% by weight). Regarding claim 5-7, 9 Askhar teaches cells preparations obtained by differentiation of pluripotent mesenchymal cells that differentiate into chondrocytes, adipocytes, fibroblasts etc., (p.6 lines 10, p.21, lines 16-28 and bridging p.22) and pluripotent cells from skin (p.20-21). Regarding claim 10 Askhar teaches cells derived from cartilages from different sites that are included (p.9, lines 10-30 and bridging). Regarding claims 11-12 Askhar teaches various compounds one or more of which are present in physiological cartilage (p.4, lines 5-15; p.6, lines 11-30 bridging p.7). Regarding claim 13-14 and 16 various additional components that could be included in therapeutic cell preparations in the form of matrix (p.14, lines 1-30). Regarding claim 17-18 Askhar teaches the use of the cell matrix or implants in therapy of various degenerative diseases of joints and cartilages in humans and animals (p.14, lines 28-31 bridging p.15, lines 1-14). Regarding claim 20-21 Askhar teaches the incubation time and bonding using hyaluronic acid in the range of 4-

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24 hrs, which is encompassed by 12-72 hr range of instant claims. The cited art thus anticipates the invention as claimed.

Conclusion:

No claim allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Kelaginamane Hiriyanna* whose telephone number is **(571) 272-3307**. The examiner can normally be reached Monday through Friday from 9 AM-5PM. Any inquiry concerning this communication or earlier communications regarding the formalities should be directed to Patent Analyst *William N. Phillips* whose telephone number is **571 272-0548**. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Joseph Woitach*, may be reached at **(571) 272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

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